REMARKS

The rejection of Claims 1-25 under 35 U.S.C. § 103(a) as unpatentable over CN 1297885 (Fan et al) in view of Bromine Compounds, and in further view of US 3,007,940 (Shavel et al), is respectfully traversed.

As recited in Claim 1 herein, an embodiment of the present invention is a process for the synthesis of gabapentin comprising the preparation of 1,1-cyclohexanediacetic acid monoamide (CHDAAM), the Hofmann transposition of the same monoamide, the purification of a gabapentin salt and the crystallization from organic solvent, wherein the preparation of the [CHDAAM] comprises:

a) the amination of 1,1-cyclohexanediacetic acid anhydride by reaction with aqueous NH_3 at a temperature lower than 30°C by using a NH_3/anhydride molar ratio lower than 3;

b) the product precipitation through the acidification of the reaction mixture, wherein the [CHDAAM] is not crystallized.

While the Examiner has previously found the presently-claimed subject matter to be patentable over the above-applied prior art, the Examiner now finds that the limitation "the [CHDAAM] is not crystallized" would have been obvious over Bromine Compounds. The Examiner relies on the disclosure at page 6, line 5 and finds that this disclosure supports a finding that crystallization is not necessary.

In reply, Applicants respectfully submit that the Examiner has misinterpreted the above-referenced part of the disclosure of Bromine Compounds. Indeed, it is clear that the crystallization step is mandatory in order to obtain an intermediate suitable for the preparation of the end-product, gabapentin. Claim 1 of Bromine Compounds itself reflects this fact. The last step thereof, i.e., step c), recites "purification of the crude CHDAAM by crystallization from a solvent." The disclosure beginning at page 6, line 5 of Bromine Compounds (first full paragraph on page 6) is drawn to the details of said step c) but there is

no disclosure therein (or anywhere else in Bromine Compounds) even suggestive that step c) is optional or a preferred embodiment of the invention therein, which is disclosed to provide an efficient "complete process for the production of CHDAAM" (page 3, first paragraph). Moreover, it is notoriously well-known in the drug art that high purity is an essential requirement in the preparation of pharmaceutically active ingredients.

Applicants wish to emphasize that the presently-claimed process can provide a product endowed with high purity, i.e., not lower than 99%, which is comparable with the one obtained in Bromine Compounds, but in the absence of a crystallization step.

Nor is the Examiner correct in finding that "by Applicant's own admission high purity is not required for transformation of the [CHDAAM] for production of gabapentin." Applicants have made no such admission and indeed, as discussed above, it is not true. Rather, as described in the specification at page 4, line 27 to page 5, line 5, suitable purity can be obtained without crystallization, making such crystallization unnecessary, but that further crystallization, even if producing an even purer product, does not lead to any industrial/advantage in the preparation of the end-product.

For purposes of completion only, it is reiterated that Fan et al and Bromine Compounds are both described in the specification herein. Fan et al requires a minimum reaction temperature for the amination of 1,1-cyclohexanediacetic acid anhydride with aqueous ammonia of from 30 to 110°C, and Bromine Compounds requires such amination be carried out in a molar ratio of ammonia/anhydride of between 5 and 10 and at a temperature below 20°C. Thus, Fan et al and Bromine Compounds each disclose the same reaction under two sets of mutually exclusive conditions, respectively. Absent the present disclosure as a guide, there would have been no reason to modify either of Fan et al or Bromine Compounds, since neither would appear to be problematical, and moreover, reaction temperature and ammonia/anhydride molar ratio would appear to be dependent on each other. In other words,

Fan et al discloses a lower molar ratio but a higher temperature, compared to Bromine Compounds. The Examiner has simply engaged in picking and choosing temperatures and ratios which support the Examiner's position, while ignoring temperatures and ratios that teach away from the present invention.

While the Examiner finds that these parameters are simply the result of optimization of result-effective properties by routine experimentation, they are not, for reasons discussed above. But even if they were, neither Fan et al nor Bromine Compounds disclose avoiding a crystallization step.

Claim 9 and claims dependent thereon are separately patentable, because none of the applied prior art discloses or suggests such a regime.

Claims 13, 14, 24 and 25 are separately patentable, because Shavel et al discloses the transformation of 1,1-cyclohexanediacetic acid into the corresponding anhydride on a steam bath (column 4, lines 40-45), and thus, not in the presence of an organic solvent.

For all the above reasons, it is respectfully requested that this rejection be withdrawn.

All of the presently-pending claims in this application are believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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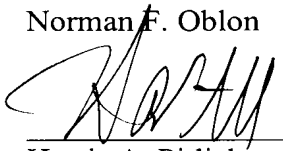

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